Office Action Summary

Application No.	Applicant(s)
09/785,881	De Barr
Examiner	**Art Unit**
Arun Chakrabarti	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Oct 5, 2001 and 2/16/01, and 6/4/01 .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-9, 16-18, and 21-25 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-9, 16-18, and 21-25 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant has elected claims 1-9, 16-18 and 21-25, corresponding to Group I, without traverse. Claims 10-15 and 19-20 have been canceled without prejudice towards further prosecution.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-9 and 21-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 2 are rejected as indefinite because the instantly claimed method lacks a final process step that clearly relates back to the preamble. For the method of claims 1 and 2, the preamble of the instantly claimed methods are drawn to a method for reducing background signals in a hybridization reaction of nucleic acids while the final process step is that of conducting a hybridization reaction using the at least two homologous probes and it is thus unclear as to whether the instantly claimed methods are drawn to a method for reducing background signals in a hybridization reaction of nucleic acids or rather conducting a

hybridization reaction using the at least two homologous probes. Method claim requires a last step or phrase in the last step that states the accomplishments of the goals for the method which were stated in the method's preamble. Claims 1 and 2 lack such a last step and are confusing because the additional method step is not sufficiently set forth. While minute details are not required in method claims, at least the basic steps must be recited in a positive, active fashions. See Ex parte Erlich, 3 USPQ2d1011, p.1011 (Bd. Pat. Applicant. Int. 1986). It is suggested that amended claims more clearly describing the intended steps be submitted.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-8, 16-17 and 21-24 are rejected under 35 U.S.C. 103 (a) over Saiki et al. (U.S. Patent 4,683,194) (July 28, 1987) in view of Bagwell et al. (U.S. Patent 5,607,834) (March 4, 1997).

Saiki et al teach a method for reducing background signals in a hybridization reaction of nucleic acids involving at least two homologous probes (Abstract and Column 6, line 65 to column 7, line 28 and Column 3, line 58 to Column 4, line 5), the method comprising:

introducing a mismatch with an intended target sequence in the probe (Column 6, line 65 to Column 7, line 15); and

conducting a hybridization reaction using the at least two homologous probes (column 7, lines 16- 28).

Saiki et al teach a method in which the homologous probes are designed to detect point mutations in at least one target sequence (Abstract and Claim 15).

Saiki et al teach a method, wherein the mismatch in a nucleotide sequence comprises 1-3 nucleotides (Column 7, lines 19-25 and Claims 16 and 21 and Figure 4).

Saiki et al teach a method, wherein the mismatch in a nucleotide sequence is located between 2 and 20 nucleotides upstream or downstream of a point mutation (Figure 4).

Saiki et al teach a method of conducting a hybridization reaction (Abstract) comprising:

mixing a set of homologous probes for detecting at least one allelic variant of a nucleic acid, wherein at least one set of homologous probes comprise at least one sequence completely complementary to and specific for one of the allelic variants of the nucleic acid, except for a

specific mismatch located downstream from the site of variation (Column 3, line 58 to Column 4, line 5 and Figure 4);

detecting variants of the nucleic acid (Column 4, lines 18-19 and Claim 15); and

using the set of homologous probes to conduct the hybridization reaction (Abstract, Claim 15 and Column 3, line 58 to Column 4, line 20 and Column 6, line 65 to column 7, line 28).

Saiki et al teach a method, wherein the nucleic acids are derived from a group of pathogens (Column 10, line 59 to column 11, line 6).

Saiki et al teach a method, wherein one of the homologous probes is provided with a detectable moiety (Figure 4).

Saiki et al do not teach a method, wherein at least one of the homologous probes is a non-linear probe.

Bagwell et al teach a method, wherein at least one of the homologous probes is a non-linear probe (Abstract and Figures 1-6).

Saiki et al do not teach a method, wherein at least one non-linear probe has a length from about 15 to about 50 nucleotides.

Bagwell et al teach a method, wherein at least one non-linear probe has a length from about 15 to about 50 nucleotides (Figure 2).

Saiki et al do not teach a method, wherein at least one non-linear probe is provided with a detectable moiety.

Bagwell et al teach a method, wherein at least one non-linear probe is provided with a detectable moiety (Abstract, Figure 7 and Claim 1).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the non-linear probe of Bagwell et al. in the method of detection of polymorphic sites in a nucleic acid sequence of Saiki et al since Bagwell et al. state, "The present invention relates to probes for use in the detection and the quantitative analysis of target molecules (Column 1, lines 9-10)". An ordinary practitioner would have been motivated to substitute and combine the non-linear probe of Bagwell et al. in the method of detection of polymorphic sites in a nucleic acid sequence of Saiki et al in order to achieve the express advantages , as noted by Bagwell et al. , of a method which provides probes for use in the detection and the quantitative analysis of target molecules.

6. Claims 1-9, 16-17, and 21-25 are rejected under 35 U.S.C. 103 (a) over Saiki et al. (U.S. Patent 4,683,194) (July 28, 1987) in view of Guo et al. (Nature Biotechnology, (1997), Vol. 15, pages 331-335).

Saiki et al teach a method for reducing background signals in a hybridization reaction of nucleic acids involving at least two homologous probes (Abstract and Column 6, line 65 to column 7, line 28 and Column 3, line 58 to Column 4, line 5), the method comprising:

introducing a mismatch with an intended target sequence in the probe (Column 6, line 65 to Column 7, line 15); and

conducting a hybridization reaction using the at least two homologous probes (column 7, lines 16- 28).

Saiki et al teach a method in which the homologous probes are designed to detect point mutations in at least one target sequence (Abstract and Claim 15).

Saiki et al teach a method, wherein the mismatch in a nucleotide sequence comprises 1-3 nucleotides (Column 7, lines 19-25 and Claims 16 and 21 and Figure 4).

Saiki et al teach a method, wherein the mismatch in a nucleotide sequence is located between 2 and 20 nucleotides upstream or downstream of a point mutation (Figure 4).

Saiki et al teach a method of conducting a hybridization reaction (Abstract) comprising:

mixing a set of homologous probes for detecting at least one allelic variant of a nucleic acid, wherein at least one set of homologous probes comprise at least one sequence completely complementary to and specific for one of the allelic variants of the nucleic acid, except for a specific mismatch located downstream from the site of variation (Column 3, line 58 to Column 4, line 5 and Figure 4);

detecting variants of the nucleic acid (Column 4, lines 18-19 and Claim 15); and

using the set of homologous probes to conduct the hybridization reaction (Abstract, Claim 15 and Column 3, line 58 to Column 4, line 20 and Column 6, line 65 to column 7, line 28).

Saiki et al teach a method, wherein the nucleic acids are derived from a group of pathogens (Column 10, line 59 to column 11, line 6).

Saiki et al teach a method, wherein one of the homologous probes is provided with a detectable moiety (Figure 4).

Saiki et al do not teach a method, further comprising amplifying a nucleic acid sequence .

Guo et al teach a method, further comprising amplifying a nucleic acid sequence (Page 331, Column 1, third paragraph and Figure 7 and Page 334, Column 1, Allele-specific PCR amplification Section).

Saiki et al do not teach a method, wherein the mismatch in a nucleotide sequence comprises 1-3 nucleotides.

Guo et al teach a method, wherein the mismatch in a nucleotide sequence comprises 1-3 nucleotides (Figure 2, legend).

Saiki et al do not teach a method, wherein at least one of the homologous probes is a non-linear probe.

Guo et al teach a method, wherein at least one of the homologous probes is a non-linear probe (Abstract and Figure 1).

Saiki et al do not teach a method, wherein at least one non-linear probe has a length from about 15 to about 50 nucleotides.

Guo et al teach a method, wherein at least one non-linear probe has a length from about 15 to about 50 nucleotides (Figures 2-5 and Table 1).

Saiki et al do not teach a method, wherein at least one non-linear probe is provided with a detectable moiety.

Guo et al teach a method, wherein at least one non-linear probe is provided with a detectable moiety (Page 335, Experimental Protocol Section, DNA sample preparation for solid-phase hybridization Subsection).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the non-linear probe of Guo et al. in the method of detection of polymorphic sites in a nucleic acid sequence of Saiki et al since Guo et al. state, "We describe an approach to increase the discrimination of single nucleotide polymorphisms (SNPs) in DNA hybridization by means of artificial mismatches. Artificial mismatches are inserted into oligonucleotide probes using the base analog 3-nitropyrrole. A significant enhancement of the discrimination is generally obtained, with a strong dependence of the enhancement on the spacing between mismatches. The improved specificity available with this strategy is demonstrated by both solid-phase hybridization analysis and allele-specific amplification within the HLA-DRB locus (Page 331, Column 1, first line of fourth paragraph to Column 2, line 2)". An ordinary practitioner would have been motivated to substitute and combine the non-linear probe of Guo et al. in the method of detection of polymorphic sites in a nucleic acid sequence of Saiki et al. in order to achieve the express advantages , as noted by Guo et al. , of a method which provides strategy to increase the discrimination of single nucleotide polymorphisms (SNPs) in DNA hybridization by means of artificial mismatches.

7. Claims 1-9, 16-18, and 21-25 are rejected under 35 U.S.C. 103 (a) over Saiki et al. (U.S. Patent 4,683,194) (July 28, 1987) in view of Guo et al. (Nature Biotechnology, (1997), Vol. 15, pages 331-335). further in view of Cronin et al. (U.S. Patent 6,027,880) (February 22, 2000) .

Saiki et al. in view of Guo et al teach the method of claims 1-9, 16-17, and 21-25 as described above.

Saiki et al. in view of Guo et al do not teach the method, wherein the nucleic acids represent a number of HIV-variants.

Cronin et al. teach the method, wherein the nucleic acids represent a number of HIV-variants (Column 18, lines 20-26).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the nucleic acids representing a number of HIV-variants of Cronin et al. in the method of detection of polymorphic sites in a nucleic acid sequence of Saiki et al in view of Guo et al., since Cronin et al. state, "Such capacity is valuable, e.g., for diagnosis of patients who are heterozygous with respect to a gene or who are infected with a virus, such as HIV, which is usually present in several polymorphic forms (Column 18, lines 23-26) ". An ordinary practitioner would have been motivated to substitute and combine the nucleic acids representing a number of HIV-variants of Cronin et al. in the method of detection of polymorphic sites in a nucleic acid sequence of Saiki et al in view of Guo et al. , as noted by Cronin et al. , of a method which provides capacity valuable for diagnosis of

patients who are heterozygous with respect to a gene or who are infected with a virus, such as HIV, which is usually present in several polymorphic forms.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703) 306-5818.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Arun Kr. Chakrabarti

Arun Chakrabarti
Patent Examiner
Art Unit 1655

October 23, 2001